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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/827,666	04/06/2001	Timothy J. Neuberger	365279-001	6738

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 08/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/827,666	NEUBERGER ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-12,19-28,34-36,46-58 and 67-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-12, 19-28, 34-36, 46-58 and 67-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. By an amendment filed January 14, 2004, claims 1-7, 13-18 and 32-33 have been cancelled; claims 8, 10, 19, 34, 46, 52, 55 and 57 have been amended; and claims 67-72 have been newly added.

Withdrawal of Allowable Subject Matter

2. The indicated allowability (pages 6-7 O.A. mailed 09/11/2003) is withdrawn in light of reconsideration of the claimed subject matter.

New Ground of Rejection

3. Applicant's arguments with respect to the claims 1-7, 13-28, 32, 33, 52-54, 57 and 58 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 8-12, 19-28, 34-36, 46-58 and 67-72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "increasing neural expression of eNCAM, MAP II, beta-tubulin, nestin, NF or NF-PO4" with the administration of N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide or "treating spinal cord injury by administering bone marrow cells from N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide-treated animal to a site of injury in animal", does not reasonably provide enablement for "promoting neural tissue

regeneration or expression", "promoting recovery of behavioral function of neurons", "treating injury to neural tissue", "inducing neuronal replacement for treating a neurodegenerative condition or disease" and "promoting regeneration of neural precursor cells", with the administration of compounds of formula (II). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are:(1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; (8) the breadth of the claims When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The instant specification discloses that the instant invention relates to promoting neural tissue regeneration or neural expression. The specification defines neural tissue as "all tissue endogenous to the nervous system" (page 13, lines 10-12 and lines 22-26); neural expression as the expression of any proteins indicative of neural tissue growth or neural tissue cell differentiation from progenitor cells (page 13, lines 13-18); and neural progenitor cells as "any cell that can differentiate into a neural tissue cell, or be induced to differentiate into a neural tissue cell, including neural precursor cells, whether directly or through intermediate cell stages"

(page 14, lines 1-3). As the specific embodiments of the invention, the instant specification discloses in-vitro study testing the activity of N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide in increasing neural expression of eNCAM, MAP II, beta-tubulin, nestin, NF and NF-PO4 (Examples 1 and 2) and in-vitro study testing the activity of N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide in increasing the growth of neurons or astrocytes (Example 4). The instant specification also discloses that animals (Fischer F344 female rats) treated with bone marrow cells from N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide-treated donor animal demonstrates a decrease in cavity size at the contusion injury site, in vivo study (Example 3).

The specification does not disclose sufficient guidance that (i) all compounds of the formula II that are potentially suitable for the invention which have been incorporated by references work similarly as to N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide. Further, the specification does not provide sufficient guidance for the skilled artisan how to ascertain (ii) which proteins indicative of neural tissue growth or neural tissue cell differentiation from progenitor cells other than the disclosed eNCAM, MAP II, beta-tubulin, nestin, NF and NF-PO4, and (iii) which neural tissues, neural precursor cells or progenitor cells other than bone marrow cells would be enabled in this invention in animals or human. Furthermore, the specification does not provide sufficient guidance for the skilled artisan how to ascertain that (iv) the growth of neuron or astrocytes by the administration of N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide in vitro would lead to the improvement of the functional recovery of neurons, and (v) provide the effective treatment of complex neurodegenerative diseases or conditions that may have unrelated manifestation in vivo, without undue amount of experimentation.

The instant invention relates to method of promoting neural tissue regeneration or expression (claims 8-12, 34-36, 57-58, 67-68); a method for promoting recovery of behavioral function of neurons (claims 19-28); a method for treating injury to neural tissue (claims 46-51, 55-56); and a method of inducing neuronal replacement for treating a neurodegenerative condition or disease (claims 52-54), wherein methods requires the administration of compounds of formula II. More specifically, claims 34-36 and 57-58 are directed to transplantation method.

The prior art recognizes the treatment of spinal cord injury by replacing damaged neural tissue with transformed cells of neural and non-neural origins, neutralizing the nerve-growth inhibitory properties of various proteins in the CNS environment, as well as introduction of stem cells or progenitor cells.

The relative skill of those in the art of pharmaceuticals is high. The unpredictability of the pharmaceutical art is very high.

As stated above, with the exception of "method of increasing neural expression of eNCAM, MAP II, beta-tubulin, nestin, NF or NF-PO4" with the administration of N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide or "treating spinal cord injury by administering bone marrow cells from N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide-treated animal to a site of injury in animal", the skilled artisan cannot envision that (a) all compounds of the formula II that are potentially suitable for the invention work similarly as to N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide; (b) the administration of N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide is capable of increasing the expression of other known neural proteins (e.g., vimentin, Sox2, Ki-67, GD2 ganglioside, MAP2ab, NeuN, FMRP, Tau, GFAP, dublecortin, CD133, CD44, CD81, CD90, CD29, NumA and etc...), and (c) promoting

regeneration of diverse neural tissues, neural precursor cells, progenitor cells or tissue of neural origin (e.g., schwanne cells, stems cells, oligodendrites, etc...) in animals or human; and (d) the administration of N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide, without neutralizing the nerve-growth inhibitory properties of various proteins in the CNS environment, is capable of providing the desired effects of the claimed invention, particularly claims 8-12, 19-28, 46-56 and 67-72 where no transplantation method is required, in animals or human.

The breath of the instant claims encompasses promotion of neural tissue (e.g., stem cells, progenitor cells, neurons, glial cells, astrocytes, oligodendrites, etc...), the expression of neural proteins (e.g., eNCAM, MAP II, beta-tubulin, nestin, NF and NF-PO4, vimentin, Sox2, Ki-67, GD2 ganglioside, MAP2ab, NeuN, FMRP, Tau, GFAP, dublecortin, CD133, CD44, CD81, CD90, CD29, NumA and etc...) or the treatment of complex neurodegenerative conditions (e.g., multiple sclerosis, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Huntington's chorea, diabetes, senile dementia, dysplasia, myelitis, spinal ataxia, Friedreich's ataxia, cerebellar cortical degenerations, Refsum's disease, abetalipoprotemia, ataxia, telangiectasia, mitochondrial multi.system disorder, transverse myelitis, anterior horn cell degeneration, such as amyotrophic lateral sclerosis, infantile spinal muscular atrophy and juvenile spinal muscular atrophy, Down's Syndrome in middle age, Diffuse Lewy body disease, Wernicke-Korsakoff syndrome, chronic alcoholism; Creutzfeldt-Jakob disease, Subacute sclerosing panencephalitis, Hallerrorden-Spatz disease, Dementia pugilistica, etc...), that are known today, and those that may be discovered in the future.

For the reason given above, in view of the nature of the invention, the amount of guidance present in the specification, the breath of the claims, the relative skill of those in the art, and the predictability or unpredictability of the art, it would take undue trials and errors to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 57-58 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: step of collecting bone marrow cells from the first mammal and delivering them to a site of injury in the first mammal or in a second mammal. Such omission leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 8-12, 19-23, 57, 67 and 69-72 are rejected under 35 U.S.C. 102(b) as being anticipated by Nair et al. (US 4965284).

Nair teaches the use of the claimed compounds including N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide for modulating the immune system; stimulating the proliferation and differentiation of blood cell progenitors in bone marrow of warm-blooded

animals (ultimately for human); accelerating the recovery of white blood cell progenitors in bone marrow of warm-blooded animals; and enhancing the activity of immune cells and/or immunoregulatory proteins, wherein said compound (composition containing said compound) is administered to warm-blood animal or warm-blood animals conditioned to chemical or irradiation therapy in amounts ranging from about 5 mg to about 400mg/kg of body weight per day, preferably from about 25mg to abut 500mg/kg of body weight per day (column 8, lines para. 1; column 12, lines 60-66; claims, especially claims 16-23).

Although Nair is silent about the instantly required " promoting neural tissue regeneration or expression" (claim 8); "the tissue is of neuronal origin and the method is for promoting neural expression" (claim 10); "the administration is effective to promote the neural expression of one or more proteins selected from the group consisting of: eNCAM, MAP II, beta-tubulin, nestin, NF and NF-PO4" (claim 12); "promoting recovery of behavioral function of neurons after a decrease in neural function" (claim 19); and "promoting regeneration of neural precursor cells" (claim 57), such properties or characteristic deem to be inherently presented in the referenced method. Where the administration of same compound (i.e., N-[4-[(4-fluorophenyl)sulfonyl]phenyl]-acetamide) at overlapping dosage amounts (i.e., about 5 mg to about 400mg/kg of body weight per day, preferably from about 25mg to abut 500mg/kg of body weight per day) to same treatment population (i.e., "warm blooded animal", "warm blooded animal" conditioned to "chemical or irradiation therapy"), the instantly claimed mechanism of action must be inherently presented in the prior art (Nair). Therefore, Nair anticipates the claimed invention.

Conclusion

7. No Claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614